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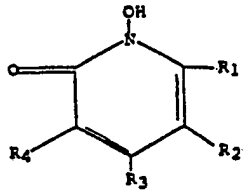
(54) Composition based on hydroxypyridone derivatives for reducing hair loss

(57) Compositions for the treatment of the hair to reduce hair-loss, comprise a medium suitable for topical application and at least one compound of the formula:



in which:

R_1 denotes a hydrogen atom, a linear or branched alkyl group having 1 to 17 carbon atoms, a cycloalkyl group having 5 to 8 carbon atoms, a cycloalkylalkylene group in which the alkylene group has 1 to 4 carbon atoms, an aryl group, an aralkyl group in which the alkyl group has 1 to 4 carbon atoms, an arylalkenyl group in which the alkenyl group has 2 to 4 carbon atoms, it being possible for the aryl groups to be substituted with an alkyl group having 1 to 4 carbon atoms or alternatively an alkoxy group having 1 to 4 carbon atoms;

R_2 denotes hydrogen, alkyl having 1 to 4 carbon atoms, alkenyl having 2 to 4 carbon atoms, a halogen atom or a benzyl radical;

R_3 denotes hydrogen, alkyl having 1 to 4 carbon atoms or phenyl; and

R_4 denotes hydrogen, alkyl having 1 to 4 carbon atoms, alkenyl having 2 to 4 carbon atoms, methoxymethyl or a halogen atom or a benzyl radical, as well as the cosmetically or pharmaceutically acceptable salts of these compounds.

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Composition based on hydroxypyridone derivatives for reducing hair loss.

The invention relates to compositions based on hydroxypyridone derivatives for reducing hair loss.

Those versed in the art have known for a long time that the natural loss of hair, in man, is an overall reflection of the balance of the hair follicles between the alternate phases of growth (anagen) and phases of loss (telogen). The average ratio of the number of follicles in the anagen phase to that in the telogen phase is of the order of 9 (90:10). It is apparent from this that the percentage of follicles in the rest phase (catagen) is very small.

The natural loss or shedding of hair may be estimated, on average, at a few hundred hairs per day for a normal physiological condition.

It is known, moreover, that certain factors, such as a hormone imbalance, a physiological stress or malnutrition, may accentuate the phenomenon.

In certain dermatoses of the scalp where there is an inflammatory feature, such as, for example, psoriasis or seborrhoeic dermatitis, hair loss may be strongly enhanced or may give rise to highly disturbed follicle cycles.

Hydroxypyridone derivatives are known per se. Among the most representative compounds, there may be

mentioned ciclopirox or 6-cyclohexyl-1-hydroxy-4-methyl-2(1H)-pyridone, known as an antifungal agent, and octopirox or 1-hydroxy-4-methyl-6-(2,4,4-trimethylpentyl)-2(1H)-pyridone, known for its antidandruff properties.

Unexpectedly, the Applicant discovered that the use of these derivatives enabled hair loss to be reduced.

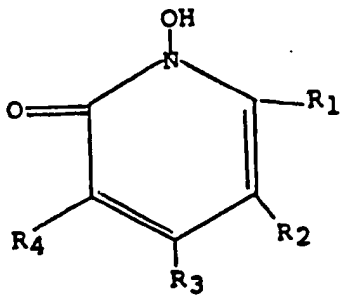
According to an especially preferred embodiment, he found that combination with steroidal or non-steroidal anti-inflammatories, such as, in particular, hydrocortisone, indomethacin, glycyrrhetinic acid, α-bisabolol, betamethasone, fluocinolone acetonide or desoxymethasone, enabled this effect to be improved further.

The subject of the invention is hence a new composition based on hydroxypyridone derivatives for reducing hair loss.

Another subject of the invention consists of their application for the treatment of the hair and the scalp.

Other subjects of the invention will become apparent on reading the description and the examples which follow.

The composition according to the invention is essentially characterized in that it contains, in a medium suitable for a topical application, at least one compound corresponding to the formula (I):



(I)

in which:

R_1 denotes a hydrogen atom, a linear or branched alkyl group having from 1 to 17 carbon atoms, a cycloalkyl group having 5 to 8 carbon atoms, a cycloalkylalkylene group, the alkylene group having from 1 to 4 carbon atoms, an aryl group, an aralkyl group, the alkyl group having from 1 to 4 carbon atoms, an arylalkenyl group, the alkenyl group having from 2 to 4 carbon atoms, it being possible for the aryl and cycloalkyl groups to be substituted with an alkyl group having 1 to 4 carbon atoms or alternatively an alkoxy group having from 1 to 4 carbon atoms;

R_2 denotes hydrogen, alkyl having from 1 to 4 carbon atoms, alkenyl having from 2 to 4 carbon atoms, a halogen atom or a benzyl radical;

R_3 denotes hydrogen, alkyl having from 1 to 4 carbon atoms or phenyl; and

R_4 denotes hydrogen, alkyl having from 1 t 4 carbon atoms, alkenyl having from 2 to 4 carbon atoms, methoxymethyl or a halogen atom or a benzyl radical, as

well as their cosmetically or pharmaceutically acceptable salts.

Among these compounds, those which are especially preferred consist of 1-hydroxy-4-methyl-6-(2,4,4-trimethylpentyl)-2(1H)-pyridone and 6-cyclohexyl-1-hydroxy-4-methyl-2(1H)-pyridone.

Among salts which are usable, there may be mentioned salts of lower alkanolamines such as ethanolamine and diethanolamine, amine or alkylamine salts and quaternary ammonium salts, as well as the salts with inorganic cations such as alkali metal, ammonium and alkaline earth metal salts.

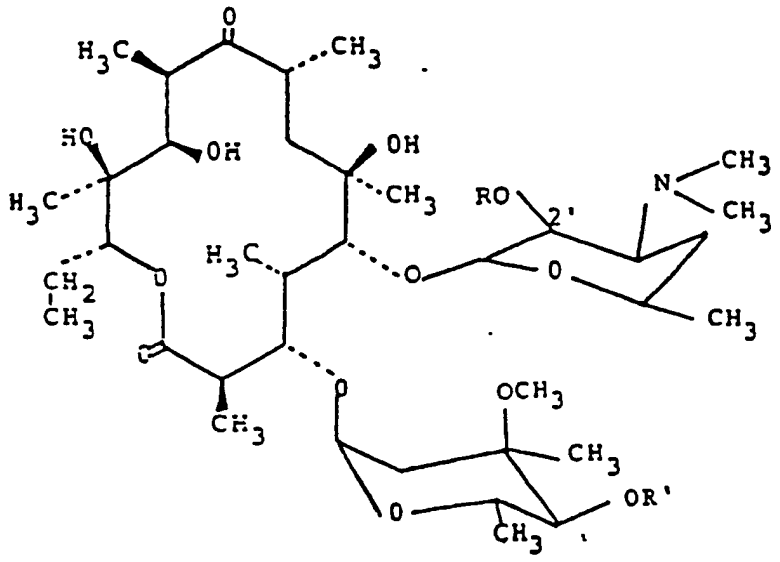
The compositions according to the invention contain, according to an especially preferred embodiment, in combination with the pyridones defined above, steroidal or non-steroidal anti-inflammatory agents such as, more especially, hydrocortisone, indomethacin, glycyrrhetinic acid, α-bisabolol, betamethasone, fluocinolone acetonide, desoxymethasone, and the like.

In another preferred embodiment of the invention, the composition contains, in addition, antibacterial agents chosen, more especially, from antibiotics of the macrolide family, and more especially erythromycin and its derivatives, and pyranosides such as lincomycin and its derivatives and clindamycin and its derivatives.

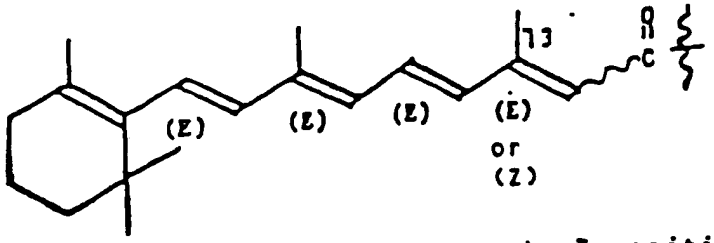
Among erythromycin derivatives, there may be mentioned, more especially, erythromycin itself, and its

derivatives such as the estolate, the ethylcarbonate, the ethylsuccinate, the glucoheptonate, the lactobionate, the propionate lauryl sulphate, the propionate, the stearate, the linoleate and monoenic esters such as erythromycin A monooleate. Among clindamycin derivatives, there may be mentioned, in addition to clindamycin itself, the hydrochloride, the palmitate and the phosphate. Among lincomycin derivatives, there may be mentioned the hydrochloride and lincomycin itself.

Other derivatives which are usable according to the invention are the retinoates of these antibiotics, and more especially all-trans and 13-cis-retinoic acid esters of erythromycin A, of lincomycin and of clindamycin and their pharmaceutically acceptable salts, as described, more especially, in the Applicant's French Patent Application No. 86/06,528. The retinoic esters at the 2'-position of erythromycin are represented more especially by the formula:

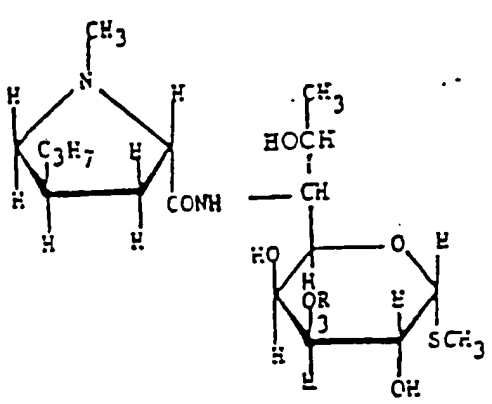


in which R denotes an all-trans-retinoyl radical or a 13-cis-retinoyl radical and R' denotes H; the retinoyl radical having the formula:

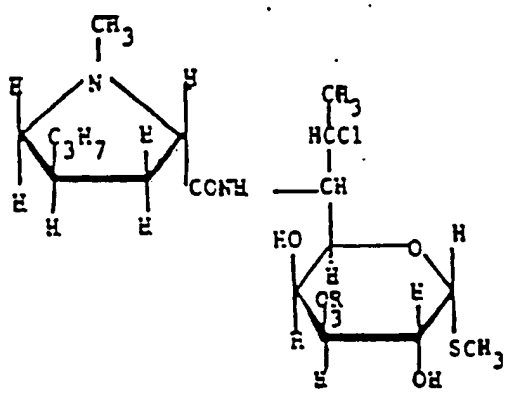


(III)

The retinoic esters at the 3-position of lincomycin and of clindamycin may be represented by the formulae:



(IV)



(V)

in which R has the same meaning as that stated above.

These various retinoic esters may be prepared according to various esterification processes, and preferably in an anhydrous organic solvent medium, especially in tetrahydrofuran alone or mixed with another organic solvent such as pyridine, by reacting an excess of mixed anhydride of carbonic and all-trans or 13-cis-retinoic acids (prepared in situ, for example, from ethyl chloroformate and all-trans or 13-cis acid) with erythromycin A, lincomycin or clindamycin in base form, in the presence of an organic or inorganic base such as pyridine and/or sodium hydrogen carbonate.

Another esterification process, in particular for lincomycin and clindamycin, consists in using the imidazolides of retinoic acids in an anhydrous solvent such as N,N-dimethylformamide, in the presence f a base such

as sodium tert-butylate or potassium tert-butylate. According to this latter process, the ester at the 7-position of lincomycin is the predominant product obtained, with esters at the 2-, 3- and 4-positions. A mixture of monoesters at the 2-, 3- and 4-positions of clindamycin is obtained in the same manner.

Other erythromycin A derivatives are represented by the formula (II), and described, in particular, in FR-A-2,582,000, in which:

R or R' denotes a di- or trienic C_{18} linear acyl radical of all-cis (Z) stereochemical configuration, and the remaining R' or R denotes a hydrogen atom.

According to a preferred embodiment, R or R' denotes the following radicals:

(9Z, 12Z)-octadecadienoyl or linoleoyl

(9Z, 12Z, 15Z)-octadecatrienoyl or α-linolenoyl, and

(6Z, 9Z, 12Z)-octadecatrienoyl or γ-linolenoyl.

2'-O-Linoleylerythromycin A, 4"-O-linoleylerythromycin A and 4"-O-(α-linoleyl)erythromycin A may be mentioned in particular.

According to the invention, the pyridones are used in compositions according to the invention in proportions of between 0.01 and 5% by weight relative to the total weight of the composition. The anti-inflammatory agents are preferably used in proportions of between 0.01 and 5% by weight for hydrocortisone or indomethacin and

α-bisabolol, and in proportions of the order of 0.001 and 0.02% by weight for the betamethasone, fluocinolone or desoxymethasone derivatives.

The antibacterial agents, in particular clindamycin, erythromycin, lincomycin or their derivatives, are preferably used in proportions of between 0.01 and 5% by weight, and especially between 0.01 and 3% by weight.

The compositions according to the invention may be presented in various forms customarily used in pharmacy or in cosmetics for the treatment of the scalp.

They may be presented, more especially, in the form of lotions, shampoos, foams, creams, gels, sticks, spray, balms, powders, or soap in cake form or liquid form. When the composition is liquid, it can comprise a medium containing water or a mixture of water and organic solvents which are acceptable from a physiological standpoint. Among these solvents, there may be mentioned lower alcohols such as ethanol and isopropyl alcohol, acetone, ethylene glycol, ethylene glycol monomethyl, monoethyl or monobutyl ethers, propylene glycol, propylene glycol monoethyl ether and dipropylene glycol monoethyl ether, C_1-C_4 alkyl esters of short-chain acids and polytetrahydrofuran ethers.

These compositions can contain thickening agents such as cellulose or cellulose derivatives, as well as heterobiopolysaccharides such as xanthan gum or polyacrylic acids crosslinked with a polyfunctional agent such as the

products sold under the name of CARBOPOL.

These compositions can also contain other adjuvants customarily used in cosmetics or in pharmacy, in particular on the scalp, and more especially surfactants, perfumes, preservative agents, pH regulators, colourings and cationic, anionic, nonionic or amphoteric polymers.

A subject of the invention also consists of the use of pyridone derivatives as defined above for the preparation of pharmaceutical compositions intended for the treatment of hair loss.

Finally, the subject of the invention is a process for the cosmetic treatment of the hair, consisting in applying on the hair at least one of the compositions as defined above, the composition having, for this purpose, an effect chiefly on the appearance of the hair.

The examples which follow are designed to illustrate the invention, no limitation of the latter being implied.

PREPARATION EXAMPLE 1

Preparation of 2'-O-(13-cis-retinoyl)erythromycin A

5 g (16.6 mmol) of 13-cis-retinoic acid are dissolved in 35 ml of anhydrous tetrahydrofuran in a round-bottomed flask and under an inert atmosphere; the reaction mixture is cooled to 0°C and then 3 ml (38 mmol) of anhydrous pyridine and 1.6 ml (16.6 mmol) of ethyl chloroformate are poured in. The solution is stirred for 5 minutes and 2.5 g (30 mmol) of sodium hydrogen carbonate are added, followed by 4.9 g (6.7 mmol) of erythromycin A, previously dissolved in 150 ml of tetrahydrofuran. The reaction mixture is then left with stirring for 10 hours while being allowed to return to room temperature (thin layer chromatography on silica gel: methylene chloride/-methanol, 10%). The solution is poured into 60 ml of water and then extracted with ethyl acetate. The organic phase is dried over magnesium sulphate, filtered and then concentrated under partial vacuum. The crude product thereby obtained is chromatographed on a column of silica gel (HPLC) using the eluant ethyl acetate/-hexane (7:3), leading to the isolation of 4.4 g (65% yield) of pure 2'-O-(13-cis-retinoyl)erythromycin A.

M.p. 82°C (hexane/ethyl acetate)

$[\alpha]_D^{22}$ = -17° (C = 6 mg/ml, dichloromethane)

Microanalysis : $C_{57}H_{93}NO_{14}$; M = 1016.4

	C	H	N
Calculated % :	67.36	9.22	1.38

Found % : 67.48 9.32 1.38

Infrared : band at 1735 cm^{-1} (ester)

^{13}C NMR ($CDCl_3$, internal ref. TMS)

Negative γ effects at the 1'-position (-2.2 ppm) and 3'-position (-2.1 ppm), indicate the 2'-position of the ester. Carbons $C"_{20}$ (20.94 ppm), $C"_{14}$ (117.28 ppm) and $C"_{12}$ (131.9 ppm) of the retinoic chain are in agreement with the 13-cis stereochemistry of the retinoic chain.

PREPARATION EXAMPLE 2

Preparation of 2'-O-(all-trans-retinoyl)erythromycin A

5 g (16.6 mmol) of all-trans-retinoic acid are dissolved in 35 ml of anhydrous tetrahydrofuran in a round-bottomed flask and under an inert atmosphere, the reaction mixture is cooled to 0°C and then 3 ml (38 mmol) of anhydrous pyridine and 1.6 ml (16.6 mmol) of ethyl chloroformate are poured in; the solution is stirred for 5 minutes and 2.5 g (30 mmol) of sodium hydrogen carbonate are added, followed by 4.9 g (6.7 mmol) of erythromycin A, previously dissolved in 150 ml of tetrahydrofuran. The reaction mixture is then left with stirring for 10 hours while being allowed to return to room temperature (thin layer chromatography on silica gel: methylene chloride/methanol, 10%). The solution is poured into 60 ml of water and then extracted with ethyl acetate. The organic phase is dried over magnesium sulphate, filtered and then concentrated under partial vaccum. The crude product

thereby obtained is chromatographed on a column of silica gel (HPLC) using the eluant ethyl acetate/hexane (7:3), leading to the isolation of 4.1 g (60% yield) of pure 2'-O-(all-trans-retinoyl)erythromycin A.

$[\alpha]_D^{22}$ = -65° (C = 2 mg/ml, dichloromethane)

Microanalysis : $C_{57}H_{93}NO_{14}.4H_2O$; M = 1088.5

	C	H	N
Calculated % :	62.89	9.35	1.29
Found % :	62.91	8.90	1.29

^{13}C NMR ($CDCl_3$, internal ref. TMS)

Negative γ effects at the 1'-position (-2 ppm) and 3'-position (-1.9 ppm), indicate the 2'-position of the ester. Carbons $C"_{20}$ (14.1 ppm), $C"_{14}$ (119.36 ppm) and $C"_{12}$ (135.19 ppm) are in agreement with the all-trans stereochemistry of the retinoic chain.

PREPARATION EXAMPLE 3

Preparation of 3-O-(all-trans-retinoyl)clindamycin

5 g (16.6 mmol) of all-trans-retinoic acid are dissolved in 30 ml of anhydrous tetrahydrofuran in a round-bottomed flask and under an inert atmosphere; the reaction mixture is cooled to 0°C and then 6 ml (76 mmol) of anhydrous pyridine and 1.6 ml (16.6 mmol) of ethyl chloroformate are poured in; the solution is stirred for 5 minutes and 1.25 g (15 mmol) of sodium hydrogen carbonate are added, followed by 2.35 g (5.5 mmol) of clindamycin, previously dissolved in 100 ml of a tetrahydrofuran/pyridine (8:2) mixture. The reaction mixture

is then left with stirring for 10 hours while being allowed to return to room temperature (thin layer chromatography on silica gel: methylene chloride/methanol 5%). The solution is poured into 80 ml of water and then extracted with ethyl acetate. The organic phase is dried over magnesium sulphate, filtered and then concentrated under partial vacuum. The crude product thereby obtained is chromatographed on a column of silica gel (HPLC) using the eluant ethyl acetate/hexane (5:5), leading to the isolation of 2.15 g (55% yield) of pure 3-O-(all-trans-retinoyl)clindamycin.

M.p. 62°C

$[\alpha]_D^{22}$ = +50° (C = 100 mg/ml, dichloromethane)

Microanalysis : $C_{38}H_{59}N_2SO_6Cl.2.5H_2O$; M = 752.5

	C	H	N
Calculated % :	60.44	8.08	3.23
Found % :	60.66	8.57	3.72

^{13}C NMR ($CDCl_3$, internal ref. TMS): negative γ effects at the 4-position (-2.8 ppm) and 2-position (-1.9 ppm). The chemical shifts of $C"_{14}$ (117.84 ppm) and $C"_{20}$ (14.11 ppm) confirm the all-trans stereochemistry of the retinoyl chain.

PREPARATION EXAMPLE 4

Preparation of 3-O-(13-cis-retinoyl)clindamycin

5 g (16.6 mmol) of 13-cis-retinoic acid are dissolved in 30 ml of anhydrous tetrahydrofuran in a round-bottomed flask and under an inert atmosphere; the reaction

mixture is cooled to 0°C and then 6 ml (76 mmol) of anhydrous pyridine and 1.6 ml (16.6 mmol) of ethyl chloroformate are poured in; the solution is stirred for 5 minutes and 1.25 g (15 mmol) of sodium hydrogen carbonate are added, followed by 2.35 g (5.5 mmol) of clindamycin, previously dissolved in 100 ml of a tetrahydrofuran/pyridine (8:2) mixture. The reaction mixture is then left with stirring for 10 hours while being allowed to return to room temperature (thin layer chromatography on silica gel; methylene chloride/methanol, 5%). The solution is poured into 80 ml of water and then extracted with ethyl acetate. The organic phase is dried over magnesium sulphate, filtered and then concentrated under partial vacuum. The crude product thereby obtained is chromatographed on a column of silica gel (HPLC) using the eluant ethyl acetate/hexane (5:5), leading to the isolation of 2 g (51% yield) of pure 3-O-(13-cis-retinoyl)-clindamycin.

M.p. 95°C (hexane/ethyl acetate)

$[\alpha]_D^{20}$ = +111° (C = 15 mg/ml, dichloromethane)

Microanalysis : $C_{38}H_{59}ClN_2SO_6$; M = 707.4

	C	H
Calculated % :	64.52	8.41
Found % :	64.47	8.45

^{13}C NMR ($CDCl_3$, internal ref. TMS)

The position of the ester is indicated by the positive β effect at the 3-position (+1.77 ppm) and the

negative γ effects at the 2-position (-1.4 ppm) and 4-position (-2.5 ppm). The 13-cis configuration is confirmed by C"20 (20.93 ppm) and C"14 (115.94 ppm).

PREPARATION EXAMPLE 5

Preparation of 3-O-(13-cis-retinoyl)lincomycin

5 g (16.6 mmol) of 13-cis-retinoic acid are dissolved in 30 ml of anhydrous tetrahydrofuran in a round-bottomed flask and under an inert atmosphere; the reaction mixture is cooled to 0°C and then 6 ml (76 mmol) of anhydrous pyridine and 1.6 ml (16.6 mmol) of ethyl chloroformate are poured in; the solution is stirred for 5 minutes and 1.25 g (15 mmol) of sodium hydrogen carbonate are added, followed by 2.2 g (5.4 mmol) of lincomycin, previously dissolved in 100 ml of a tetrahydrofuran/pyridin (7:3) mixture. The reaction mixture is then left with stirring for 10 hours while being allowed to return to room temperature (thin layer chromatography on silica gel: methylene chloride/methanol, 10%). The solution is poured into 100 ml of water and then extracted with ethyl acetate. The organic phase is dried over magnesium sulphate, filtered and then concentrated under partial vacuum. The crude product thereby obtained is chromatographed on a column of silica gel (HPLC) using the eluant ethyl acetate/hexane (8:2), leading to the isolation of 1.85 g (50% yield) of pure 3-O-(13-cis-retinoyl)lincomycin.

M.p. 95° (hexane/ethyl acetate)

$[\alpha]_D^{20}$ = +103° (C = 7 mg/ml, dichloromethan·)

Microanalysis : $C_{38}H_{60}N_2SO_7.2.5H_2O$; M = 734.5

	C	H
Calculated % :	62.18	9.03
Found % :	62.33	8.64

^{13}C NMR ($CDCl_3$, internal ref. TMS)

The position of the ester is indicated by the positive β effect at the 3-position (+1.6 ppm) and the negative γ effects at the 2-position (-2.4 ppm) and 4-position (-1.9 ppm). The 13-cis configuration is confirmed by C"20 (20.98 ppm) and C"14 (115.83 ppm).

PREPARATION EXAMPLE 6

Preparation of a mixture of 7-O-(all-trans-retinoyl)lincomycin, 3-O-(all-trans-retinoyl)lincomycin and 2-O-(all-trans-retinoyl)lincomycin monoesters

30 g (74 mmol) of lincomycin are dissolved in 300 ml of anhydrous N,N-dimethylformamide in a round-bottomed flask and under an inert atmosphere, 830 mg (7.4 mmol) of potassium tert-butylate are then added and stirring is continued at room temperature for 90 minutes. A solution of 13 g (37 mmol) of 1-(all-trans-retinoyl)imidazole in 150 ml of N,N-dimethylformamide is then poured in and the resulting medium is stirred at room temperature for 12 hours (thin layer chromatography on silica gel: methylene chloride/methanol, 7.5%). The solution is poured into 500 ml of water and then extracted with ethyl acetate. The organic phase is dried over magnesium sulphate, filtered and then concentrated under partial vacuum.

The crude product thereby obtained is chromatographed on a column of silica gel (HPLC) using the eluant ethyl acetate/hexane (7:3), leading to the isolation of 39 g (77%) of a mixture of all-trans-retinoic monoesters of lincomycin at the 2-, 3- and 7-positions.

^{13}C NMR ($CDCl_3$, internal ref. TMS)

- Negative γ effects at the 8-position (-2.5 ppm) and the 6-position (-3.8 ppm) indicate the site of esterification of a monoester at the 7-position,
- Negative γ effect at the 1-position (-4 ppm) indicates the monoester at the 2-position, and negative γ effects at the 2-position (-2 ppm) and 4-position (-2.6 ppm) indicate the position of the monoester at the 3-position.

The positions of C_1 are at 85.06 ppm for the 2-monoester, at 88.45 ppm for the 7-monoester and at 89.67 ppm for the monoester at the 3-position.

The all-trans configuration of the retinoic chain is indicated for C"14 at 117.78 ppm and for C"20 at 14.08 ppm; a trace of isomerization is noted by the presence of a peak at 115.2 ppm (C"14) indicating the 13-cis isomer.

PREPARATION EXAMPLE 7

Preparation of a mixture of 2-O-(all-trans-retinoyl)clindamycin, 3-O-(all-trans-retinoyl)clindamycin and 4-O-(all-trans-retinoyl)clindamycin monoesters

20 g (47 mmol) of clindamycin are dissolved in 250 ml of an anhydrous N,N-dimethylformamide in a round-

bottomed flask and under an inert atmosphere, and 527 mg (4.7 mmol) of potassium tert-butylate are then added to the reaction medium, which is then stirred at room temperature for 90 minutes. A solution of 8.250 g (23.5 mmol) of 1-(all-trans-retinoyl)imidazole in 150 ml of anhydrous N,N-dimethylformamide is then poured in and the resulting medium is stirred at room temperature for 12 hours (thin layer chromatography on silica gel: methylene chloride/methanol, 5%). The solution is then poured into 500 ml of water, after which it is extracted with ethyl acetate. The organic phase is dried over magnesium sulphate, filtered and then concentrated under partial vacuum. The crude product thereby obtained is chromatographed on a column of silica gel (HPLC) using the eluant ethyl acetate/hexane (5:5), leading to the isolation of 28 g (85%) of a mixture of all-trans-retinoic monoesters of clindamycin at the 2-, 3- and 4-positions.

^{13}C NMR ($CDCl_3$, internal ref. TMS)

- Negative γ effect at the 1-position (-3 ppm) indicates the 2-position of the ester,
- Negative γ effects at the 4-position (-2.8 ppm) and 2-position (-1.9 ppm) indicate the monoester at the 3-position, and weak negative γ effect at the 3-position indicates the monoester at the 4-position.

The positions of C_1 are at 84.63 ppm for the 2-monoester, at 88.79 ppm for the 3-monoester and at 87.98 ppm for the 4-monoester.

The all-trans configuration of the retinoic chain is predominant ($C"_{14}$ at 117.5 ppm and $C"_{20}$ at 14.08 ppm), but there are clear traces of isomerization, in particular at $C"_{20}$ and $C"_{14}$.

EXAMPLE 1

SHAMPOO COUNTERACTING HAIR LOSS (for frequent use)

Sodium lauryl ether sulphate		7	g
Hydroxyethylcellulose		2	g
Clindamycin		0.4	g
Octopirox		0.5	g
α-Bisabolol		0.75	g
Butylated hydroxytoluene (BHT)		0.3	g
Perfume		0.05	g
Triethanolamine qs	pH 6.5		
H_2O qs		100	g

EXAMPLE 2

TREATMENT SHAMPOO COUNTERACTING HAIR LOSS

Nonionic surfactant obtained by condensation of 3.5 mol of glycidol with a C_{11}-C_{14} α diol according to FR 2,091,516	12.5	g
Linoleic ester of erythromycin	1	g
Octopirox	0.5	g
Hydrocortisone	0.5	g
BHT	0.2	g
H_2O qs	100	g

EXAMPLE 3

LOTION COUNTERACTING HAIR LOSS (non-rinsed product)

Clindamycin	0.5	g
Ciclopirox	0.5	g
Hydrocortisone	0.2	g
Perfume	0.05	g
Water/ethanol (70:30 V/V) qs	100	g

EXAMPLE 4

FOAMING GEL COUNTERACTING HAIR LOSS

Triethanolamine lauryl ether sulphate	8 g
Carbopol	.2 g
Sodium chloride	2 g
Glycerol	3 g
Glycyrrhetinic acid	1.5 g
Octopirox	0.8 g
All-trans-retinoic ester of erythromycin	0.05 g
BHT	0.3 g
H_2O qs	100 g

EXAMPLE 5

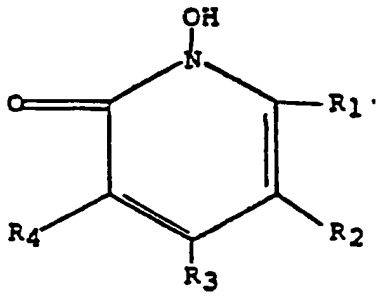
HAIRSPRAY COUNTERACTING HAIR LOSS

Ethanol	30 g
Xanthan gum sold by the company KELCO under the name of Keltrol	2 g
Octopirox	0.5 g
Linolenic ester of erythromycin	1 g
BHT	0.2 g
Perfume	0.05 g
H_2O qs	100 g

This composition is packaged in a conventional aerosol device in the presence of 6 g of a propellant consisting of a mixture of FREON 12 and 114 (40:60).

CLAIMS

1. A composition suitable for topical application which comprises at least one compound corresponding to the formula:



(I)

in which:

R_1 denotes hydrogen, linear or branched alkyl having 1 to 17 carbon atoms, cycloalkyl having 5 to 8 carbon atoms, cycloalkylalkylene in which the alkylene group has 1 to 4 carbon atoms, aryl, aralkyl in which the alkyl group has 1 to 4 carbon atoms or arylalkenyl in which the alkenyl group has 2 to 4 carbon atoms, such that the cycloalkyl and aryl groups can be substituted by an alkyl or alkoxy group having 1 to 4 carbon atoms;

R_2 denotes hydrogen, alkyl having 1 to 4 carbon atoms, alkenyl having 2 to 4 carbon atoms, halogen or benzyl;

R_3 denotes hydrogen, alkyl having 1 to 4 carbon atoms or phenyl; and

R_4 denotes hydrogen, alkyl having 1 to 4 carbon atoms, alkenyl having 2 to 4 carbon atoms, methoxymethyl, halogen or benzyl, or a cosmetically or pharmaceutically acceptable salt thereof.

2. A composition according to claim 1, which contains 1-hydroxy-4-methyl-6-(2,4,4-trimethyl-pentyl)-2(1H)-pyridone and 6-cyclohexyl-1-hydroxy-4-methyl-2(1H)-pyridone.

3. A composition according to claim 1 or 2, which also contains at least one stercidal or non-steroidal anti-inflammatory agent.

4. A composition according to claim 3, in which the anti-inflammatory agent is hydrocortisone, indomethacin, glycyrrhetinic acid, α-bisabolol, betamethasone, fluocinolone acetonide or desoxymethasone.

5. A composition according to any one of claims 1 to 4 which also contains at least one antibacterial agent which is a macrolide or pyranoside.

6. A composition according to claim 5, in which the macrolide is erythromycin or a derivative thereof and/or the pyranoside is lincomycin or clindamycin or a derivative thereof.

7. A composition according to claim 6, in which the erythromycin derivative is the estolate, ethylcarbonate, ethylsuccinate, glucoheptonate, lactobionate, propionate lauryl sulphate, propionate, stearate, linoleate or monoenic, di- or trienic ester of erythromycin, and/or the clindamycin derivative is the hydrochloride, palmitate or phosphate, and/or the lincomycin derivative is a hydrochloride.

8. A composition according to any one of claims 5 to 7, in which the erythromycin, lincomycin or clindamycin derivative is the all-trans- or 13-cis-retinoic acid ester of erythromycin A, lincomycin or clindamycin, or a pharmaceutically or cosmetically acceptable salt thereof.

9. A composition according to any one of claims 1 to 8, in which the pyridone derivative is present in an amount from 0.01 to 5% by weight relative to the total weight of the composition.

10. A composition according to any one of claims 5 to 9, in which the antibacterial agent is present in an amount from 0.01 to 5% by weight.

11. A composition according to claim 10, in which the antibacterial agent is present in an amount from 0.01 to 3% by weight.

12. A composition according to any one of claims 3 to 11, in which the anti-inflammatory agent is present in an amount from 0.01 to 5% by weight if it is hydrocortisone, indomethacin or α-bisabolol, and in an amount from 0.001 to 0.02% by weight if it is betamethasone, fluocinolone or a desoxymethasone derivative.

13. A composition according to any one of claims 1 to 12 which is in the form of a lotion, shampoo, foam, cream, gel, stick, spray or balm.

14. A composition according to any one of claims 1 t 13, in which the medium suitable f r topical application

consists of water or a mixture of water and at least one physiologically acceptable solvent.

15. A composition according to any one of claims 1 to 14 which also contains one or more thickening agents, surfactants, preservative agents, pH regulators, colourings, cationic, anionic, nonionic or amphoteric polymers or perfumes.

16. A composition according to claim 1 substantially as described in any one of Examples 1 to 5.

17. Process for the cosmetic treatment of the hair which comprises applying thereto at least one composition as claimed in any one of claims 1 to 16.

18. Use of the composition as defined in any one of claims 1 to 16, for the preparation of a composition intended for the pharmaceutical treatment of hair loss.

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